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Fistula dysfunction: Effect on rapid hemodialysis

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Fistula dysfunction: Effect on rapid hemodialysis. Rapid hemodialysis (Qb 400 to 500 ml/min) places considerable demands on hemodialysis vascular access. This six-month prospective study enrolled 52 patients and evaluated urea recirculation as a means of detecting fistula dysfunction. It evaluated the effects of fistula location and dialysis blood flow on urea recirculation during rapid hemodialysis and assessed the effect of rapid dialysis on fistula thrombosis. Urea recirculation increased as Qb increased from 300 to 400 ml/min (8 ± 3% to 16 ± 3%, $P < 0.05$). The extent of urea recirculation was also fistula site dependent (radial fistulas 18 ± 4%, upper arm fistulas 11 ± 3%, Qb 400 ml/min, $P < 0.05$). Site and blood flow dependent urea recirculations were an indicator of venous stenoses. When venous stenoses were corrected, urea recirculation rates improved (36 ± 3% to 21 ± 3%, $P < 0.05$). There were no differences between methods of determining urea recirculation early in dialysis (contralateral arm venepuncture vs. stop flow technique; 30 to 60 min). However, at 120 minutes urea recirculation was significantly greater with the contralateral arm venepuncture technique. Venous dialysis pressure at Qb 400 ml/min had limited use as a predictor of venous stenoses unlike its value at lower Qb. Fistula thrombosis (0.26/patient year of dialysis) and fistula replacement (0.09/patient year of dialysis) were similar to our observations in a conventional hemodialysis facility where prospective correction of fistula dysfunction was also used.

Provision of long-term renal replacement therapy by hemodialysis depends upon reliable patent access to the circulation. Currently vascular access for hemodialysis is provided by the use of endogenous (native) or synthetic arteriovenous fistulas [1–4]. This access to the circulation represents the "weakest link" in modern dialytic therapy. Conversion from conventional (Qb 200 to 300 ml/min) to rapid (Qb 400 to 500 ml/min) hemodialysis has placed considerable demands on hemodialysis vascular access both in terms of fistula durability and fistula function. Questions of fistula patency and function in rapid hemodialysis have not been systematically addressed.

Preventive care of vascular access is gaining favor. We have shown that prospective detection and correction of venous stenoses improves fistula patency and decreases thrombosis rates [4]. Venous dialysis pressure provides a useful index for prospectively detecting venous stenoses during conventional hemodialysis (Qb 200 to 300 ml/min) but has been difficult to adapt to the higher blood flows used in rapid dialysis [4]. Windus and associates described urea nitrogen recirculation ratios as a potential mechanism of detecting patients with inadequate fistula function during rapid hemodialysis [5]. Sherman and Levy described increased urea recirculation with increasing Qb and raised questions of decreasing dialysis efficiency at faster blood flow rates [6].

Despite these observations fundamental questions concerning vascular access and rapid hemodialysis remain unanswered. We designed this study to focus on some of these unresolved issues: (1.) the effect of fistula location on urea recirculation during rapid hemodialysis; (2.) the development of prospective methods to detect venous stenosis in the dialysis circulation during rapid hemodialysis; and (3.) the effect of rapid dialysis on fistula thrombosis.

Methods

Patients

Fifty-two maintenance hemodialysis patients (22 males, 30 females) from the REN Dialysis Center in Henderson, North Carolina were enrolled in this study. Forty-five patients were Black, seven patients were White, mean age 54 ± 6. Patients enrolled in the study were prospectively followed for six months. Fifty patients (96%) were receiving EPO (mean Hct 29). Four patients at the center declined to participate in the study.

There were 27 radial artery fistulas, 22 were synthetic, 5 were primary AV fistulas. There were 15 loop synthetic fistulas originating in the lower brachial artery in the area of the antecubital fossa with the fistula loop extending down into the forearm and anastomosing above the antecubital fossa. These are termed brachial fistulas. There were 10 upper arm synthetic fistulas. The arterial anastomosis in these fistulas was either the upper brachial or the axillary artery with the venous anastomosis occurring in the upper arm. Forty-four of the 47 synthetic fistulas were 6 mm in diameter. The diameter of three synthetic fistulas inserted at other centers was unknown. One of five surgeons placed all but three fistulas.

Venous dialysis pressures were measured 30 minutes into each hemodialysis treatment at blood flows of 400 ml/min through 15 gauge needles (Terumo Inc., 1 inch needle length). Pressure >240 mm Hg present on three consecutive treatments was considered abnormal. This value was chosen based on analysis of data from previous studies at similar blood flows [4, 7, 8]. Abnormal values were referred for elective fistulography. Our previous protocol using Qb 200 to 225 for the first 30 minutes of the treatment was not used in this study because of

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Table 1. Urea recirculation analysis, Qb 400 ml/min

Dialysis duration	Stop-flow technique	Contralateral arm technique
30 minutes	16 ± 3	17 ± 3
60 minutes	17 ± 2	17 ± 3
120 minutes	19 ± 3	24 ± 4[a]

[a] $P < 0.05$

its adverse impact on treatment duration [4, 9, 10]. When employed it has successfully predicted venous stenoses [9].

Monthly urea nitrogen recirculation ratios were performed during the first hour of the treatment (majority performed at 30-min target time) using a three-sample technique, with the peripheral sample being obtained by venipuncture in the contralateral arm [5]. Efforts were made to keep the needles as far apart as possible but a set distance was not employed. Distances between needles was at least 5 cm. Arterial needles were pointed at the arterial anastomosis and venous needles at the distal vein.

Stop flow technique was compared with contralateral arm venepuncture technique at 30, 60, and 120 minutes. There were no significant differences at 30 or 60 minutes into the treatment with technique or time of measurement. However, at 120 minutes into the treatment both techniques showed higher recirculation than earlier measurements (Table 1) with the contralateral arm method being significantly greater. Based on these observations urea recirculation is reported only at 30 to 60 minutes into the treatment for all other comparisons unless otherwise stated.

Urea recirculation was calculated using a standard formula (peripheral − arterial) divided by (peripheral − venous) times 100 = % recirculation. Arterial and venous samples were drawn from pre- and post-kidney near simultaneously with the peripheral samples obtained by immediate contralateral arm venepuncture or stop flow method. Stop flow method was performed by stopping the blood pump and clamping the arterial (pre-kidney) line and flushing the arterial line to the patient until clear. After 60 seconds a sample was drawn from the arterial line after the flushed saline was withdrawn from the line. Recirculation ratios >15% were repeated and if elevated on repeat the patients referred for elective fistulogram and possible angioplasty of the vascular access. Patients with recirculation greater than 15% but no stenosis at fistulogram were not restudied unless recirculation increased greater than 10% or venous dialysis pressures increased as outlined. Following angioplasty, repeat recirculation ratios were performed to detect any improvement.

Urea recirculation tests were performed on the entire hemodialysis population monthly, at the initiation of the study and following any intervention. Data was analyzed by Qb and by type and location of fistula. Fistulograms and fistula angioplasty were performed at the Duke Medical Center as previously described [4, 7, 8]. Intravascular ultrasound (IVUS) was employed to aid in assessment of degree of stenosis and to analyze results of angioplasty [11].

Thromboses, surgical revisions and angioplasty were tallied. Data were analyzed with a paired Student *t*-test for paired data and with an unpaired Student *t*-test for unpaired data. Data are reported as mean values ± standard error of the mean.

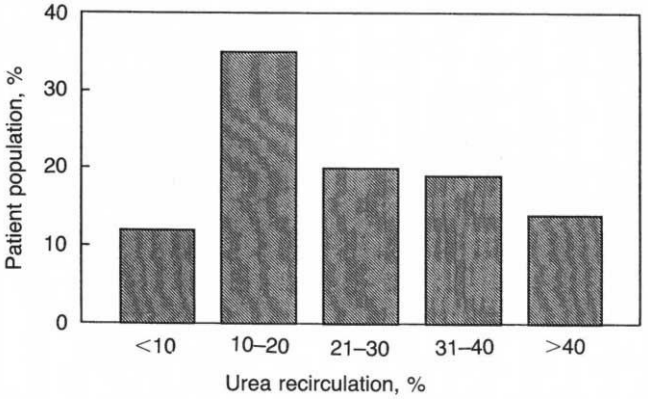

Fig. 1. *Urea recirculation in patients at the initiation of the study (Qb 400 ml/min) prior to correction of venous stenoses.*

Results

Techniques of measuring urea recirculation (1. contralateral arm venepuncture, 2. stop flow method) were compared (Table 1). Measurements at 30 and 60 minutes were not different either between methods or between times of measurement. In contrast, at 120 minutes both methods showed trends toward greater values than obtained at earlier determinations. Contralateral arm venepuncture was significantly greater than both earlier values and values obtained at 120 minutes with stop flow method ($P < 0.05$; Table 1). Unless otherwise stated all measurements of urea recirculation were performed by contralateral arm venepuncture at 30 to 60 minutes into the treatment (target time 30 min).

The mean recirculation ratio at the initiation of the study prior to any prospective correction of venous stenoses was 25 ± 4% (range 3 to 57% Qb 400 ml/min). Figure 1 depicts the distribution of urea recirculation ratios at the start of the study. This fell to 17 ± 3% at the end of the study associated with correction of venous stenoses.

The effect of blood flow on urea recirculation was tested in the entire hemodialysis population. These measurements were performed at 30 minutes into the treatment on consecutive dialysis treatments after the conclusion of the study. Previous abnormal urea recirculations had been evaluated with venography and angioplasty earlier in the study. Hence, to the best of our ability preexisting venous stenoses had been corrected. Flow dependent urea recirculation was demonstrated (Qb 300 ml/min 8 ± 3%, Qb 400 ml/min 16 ± 3%, $P < 0.05$). Analysis of urea recirculation by fistula location and Qb is represented in Table 2. Increases in blood flow increased urea recirculation. The effect was most dramatic in radial fistulas where urea recirculation ratios increased from 8 ± 2 to 18 ± 4% ($P < 0.05$). Brachial fistulas showed less effect, increasing from 7 ± 3 to 15 ± 2% ($P < 0.05$). The effects were insignificant in upper arm fistulas increasing from 7 ± 2% to 11 ± 3% (P = NS). At blood flows of 300 ml/min there were no statistical differences in recirculation ratios in any of the three anatomic locations (P = NS).

Table 3 examines the detection of venous stenoses at blood flows of 400 ml/min by the use of urea recirculation ratios. Five patients were studied with recirculation ratios between 15 to 19%. Only one patient had a >50% stenosis at the time of study

Table 2. Analysis of urea recirculation by fistula location

Fistula location	Qb 300 ml/min	Qb 400 ml/min
Radial	8 ± 2%	18 ± 4%[a]
Brachial	7 ± 3%	15 ± 2%[a]
Upper arm	7 ± 2%	11 ± 3%

[a] $P < 0.05$

Table 3. Detection of venous stenoses (Qb 400 ml/min)

% Recirculation	Fistulograms	50% Stenosis	True positives	False positives
15–19	5	1	20%	80%
20–30	12	7	58%	42%
31–40	11	9	82%	18%
>40	10	10	100%	0%

leading to a true positive rate of 20%. At recirculations of 20 to 30%, twelve patients were studied and seven high grade stenoses were detected leading to a true positive rate for detection of stenoses of 58%. As the percent recirculation increased to 31 to 40%, the yield for high grade stenoses increased to 82%. By recirculation >40%, all ten patients studied had >50% stenoses. Thus, recirculation ratios were predictive of venous stenoses. The predictive value increased as the urea recirculation increased. Overall, urea recirculation >20% had a 79% likelihood of detecting significant venous stenoses.

Figure 2 shows the effect of correction of venous stenoses on urea recirculation. During the study, 32 patients underwent percutaneous transluminal angioplasty for >50% venous stenoses. Mean recirculation pre-angioplasty was 38 ± 4%; this decreased to 21 ± 3% post-angioplasty ($P < 0.05$), documenting that correction of venous stenosis decreased urea recirculation and improved the efficiency of hemodialysis. At the end of the study the mean recirculation ratio in the population (Qb 400 ml/min) was 17 ± 3% ($P < 0.05$) compared to 25 ± 4% at the beginning of the study.

The mean venous dialysis pressure in the entire patient population measured at Qb 400 ml/min was 190 ± 8 mm Hg (range 140 to 255 mm Hg). Mean venous dialysis pressure in patients with a documented 50% stenosis was 216 ± 09 mm Hg. This was not statistically different from the population as a whole (190 ± 08 mm Hg, P = NS). Venous dialysis pressures >240 mm Hg were associated with venous stenosis in 80% of instances (4 of 5 cases). All five patients also had recirculation >20%. At blood flows of 400 ml/min, in patients with venous dialysis pressure of <240 mm Hg, the overlap of normals with patients with stenoses made venous dialysis pressure of limited use as a clinical tool.

Prospective monitoring and correction of venous stenoses was performed during this study. Using these techniques there were six thromboses representing 0.26 thromboses/patient year of dialysis. There were two replaced fistulas representing 0.09 fistulas replaced/patient year of dialysis. There were no fistulas lost during the study secondary to infection. In addition, two fistulas were electively revised. Both were primary AV fistulas that were unable to reach target blood flow rates of 300 ml/min. During the course of the study 38 fistulograms were performed in 32 patients.

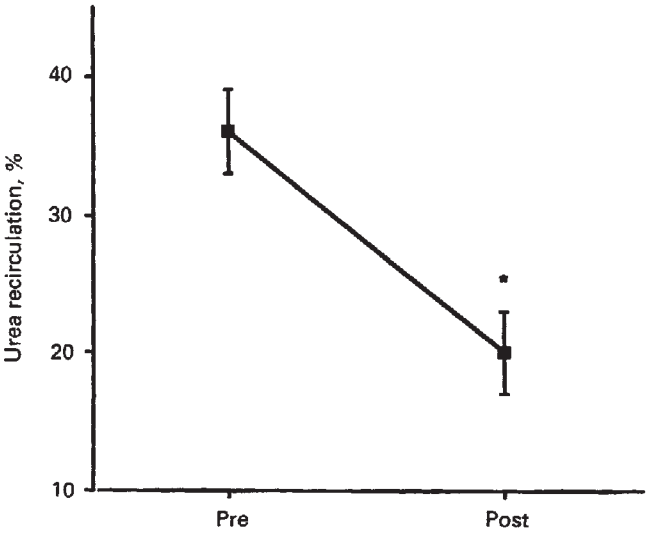

Fig. 2. *Urea recirculation pre- and post-transluminal angioplasty in patients with >50% hemodialysis fistula venous stenoses.* * $P < 0.05$

Discussion

Vascular access continues to be the Achilles' heel of modern hemodialysis. Conversion from conventional (Qb 200 to 300 ml/min) to rapid hemodialysis (Qb 400 to 500 ml/min) has placed significant additional demands on hemodialysis vascular access. Questions of fistula durability and patency under these conditions have not been systematically addressed.

In 1987, we noted that venous dialysis pressure measured at blood flows of 200 to 225 ml/min could predict outflow stenoses in hemodialysis fistulas [8]. We subsequently showed that prospective correction of these venous stenoses with transluminal angioplasty or surgical revision significantly improved hemodialysis fistula patency and significantly decreased thrombosis rates [4]. However, we also noted when blood flows were increased beyond 225 ml/min venous dialysis pressure lost much of its predictive ability [4, 9]. Recently several investigators have suggested that correlation of venous dialysis pressure with venous stenosis may be most accurate at Qb 0 [12]. Methods and equipment to measure venous dialysis pressure at Qb 0 have yet to be tested in a clinical trial. Keeping Qb at 200 ml/min for 30 minutes or more at each treatment is predictive of venous stenoses [9] but works against the purpose of rapid dialysis.

In 1990, Windus and associates demonstrated that elevated urea recirculation during rapid hemodialysis could be used to predict fistula dysfunction. They demonstrated that urea recirculation decreased following correction of venous stenosis with transluminal angioplasty [5]. Sherman and Levy documented that urea recirculation increased significantly when Qb was increased from 50 to 300 ml/min in 16 patients [6]. Observations in our current study with 54 patients prospectively evaluated over a six month interval confirm and extend the observations of both groups of investigators while raising the new issue of site specific recirculation. In addition, this current trial addresses the issue of thrombosis and fistula loss during rapid hemodialysis.

This study demonstrates that urea recirculation is a valuable tool both for detecting venous stenoses and for evaluating the efficiency of rapid hemodialysis. However, urea recirculation must be interpreted carefully. As shown in this study and as predicted by other investigators the method and time of collection has a significant impact upon the data obtained [13–15]. Both stop flow and contralateral arm venepuncture techniques are reliable early in the dialysis treatment. However, by 120 minutes recirculation increases with both methods probably associated with falling vascular volume and decreasing cardiac output associated with volume removal [13]. Contralateral arm venepuncture shows significantly increased recirculation possibly because of peripheral slowing or sludging of venous flow in the contralateral arm [14]. Differences between peripheral vein and artery urea during hemodialysis support these observations [14]. Based on these observations urea recirculation seems most reliable when measured at a known Qb within 60 minutes of initiating hemodialysis.

Fistula location has a effect on Qb dependent urea recirculation at blood flows of 400 ml/min. Radial fistulas showed the largest increments in recirculation as blood flows increased. In contrast, upper arm fistulas showed insignificant increments in recirculation associated with increasing Qb. These observations provide additional reasons to explain differences between theoretic and calculated Kt/V. The need to actually calculate rather than extrapolate urea reduction and Kt/V is readily apparent. Individual fistulas showed variability within groups. Several radial fistulas exhibited limited recirculation. Nonetheless, as a group, Qb-dependent recirculation was significantly higher in radial fistulas.

The necessity of maintaining access patency and preserving the maximum number of access sites for our patients' lifetime mandates placement of fistulae as distal as possible as long as possible on the extremity. Fistula placements proceed more proximally up the limb only as the more distal sites are exhausted. The elevated recirculation ratios shown in radial fistulas suggest that longer durations of dialysis may be warranted in many patients.

The ability to detect upstream venous stenosis by the use of elevated recirculation ratios has been previously established [5, 9]. However, it is obvious that the location of the fistula as well as the blood flow rate has an impact on the interpretation of what should be considered a normal or abnormal recirculation ratio for purposes of detecting venous stenoses. Traditionally, recirculation ratios in excess of 15% have been considered abnormal. In this hemodialysis population at an extracorporeal Qb of 400 ml/min, venous stenoses were detected only 20% of the time with recirculation of 15 to 19%. As urea recirculations increased, the likelihood of detecting an upstream stenosis increased. By urea recirculations of 40%, there was a 100% likelihood in the study population of having a significant abnormality in venous outflow. This study demonstrates that site and Qb specific interpretation of urea recirculation is required. Interpretation of our data suggests that at Qb 400 ml/min a more precise indicator of fistula dysfunction in most fistulas is a urea recirculation of 20%.

Following percutaneous transluminal angioplasty recirculation ratios fell significantly. Thus, correction of stenoses decreases recirculation. The thrombosis rate 0.26/patient year and fistula loss rate 0.09/patient year, in this study, are similar to our previously published observations in a conventional hemodialysis facility where prospective detection and correction of venous stenoses were also employed (0.20 thromboses/patient year, 0.07 fistula replacements/patient year) [4]. Observations from our center prior to preventive therapy revealed poorer fistula patency (0.61 thromboses/patient year, 0.26 fistula losses/patient year) [4]. When prospective techniques of detection and correction are employed, the thrombosis and fistula loss rates are comparable between conventional and rapid hemodialysis.

In summary, urea recirculation is blood flow and fistula location dependent. When appropriately performed and interpreted urea recirculation serves as a useful mechanism for the detection of venous stenoses. When stenoses are corrected, recirculation decreases significantly. Efficiency of rapid dialysis is fistula dependant. When prospective techniques of detection and correction of venous stenosis are employed, the fistula loss and thrombosis rate of a facility employing rapid hemodialysis is similar to a facility employing conventional hemodialysis.

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